Australian Government

Medical Services Advisory Committee

Public Summary Document

Application No. 1524 – BRAF testing for dabrafenib/trametinib in Stage III melanoma

Applicant: **Novartis Australia Pty Ltd**

Date of MSAC consideration: **MSAC 76th Meeting, 1-2 August 2019**

Context for decision: MSAC makes its advice in accordance with its Terms of Reference, visit the MSAC website

1. Purpose of application

An application to broaden the existing Medicare Benefits Schedule (MBS) item for *BRAF* V600 testing to include Stage III resected melanoma patients was received from Novartis Australia by the Department of Health.

2. MSAC's advice to the Minister

After considering the strength of the available evidence in relation to comparative safety, clinical effectiveness and cost-effectiveness, MSAC supported the requested amendment to the MBS item descriptor for 73336 to omit the word "unresectable" in relation to Stage III melanoma, because the performance of the test is expected to be the same in the additional patients who would be tested, and the additional costs would be justified by those who would become eligible for earlier treatment with dabrafenib in combination with trametinib.

Consumer summary
Novartis Australia Pty Ltd applied to have the word "unresectable" (that is, cannot be removed completely by surgery) removed from the Medicare Benefits Schedule (MBS) item which relates to testing for *BRAF* gene mutation in patients with stage III or stage IV melanoma. Removing the word "unresectable" means funding would be available for patients with Stage III melanoma who have had surgery to be tested for BRAF gene mutations; the most common mutation is called V600. The test result would identify the need for drug treatment to target V600. The Pharmaceutical Benefits Advisory Committee has recently recommended extending an existing listing on the Pharmaceutical Benefits Scheme (PBS) for a medicine that targets V600 (dabrafenib). Currently, patients with unresectable Stage III or Stage IV metastatic cutaneous melanoma whose tumour tissue cells have the *BRAF* V600 mutation are eligible for PBS-funded treatment with dabrafenib (given in combination with trametinib).

Consumer summary
MSAC's recommendation to the Commonwealth Health Minister MSAC agreed to remove the word "unresectable" from the MBS item descriptor.

3. Summary of consideration and rationale for MSAC's advice

MSAC noted that Application 1524 is part of a streamlined codependent submission seeking to extend MBS item 73336 to include patients with completely resected Stage III metastatic cutaneous melanoma alongside a corresponding request to the Pharmaceutical Benefits Advisory Committee (PBAC) to extend the Pharmaceutical Benefits Scheme (PBS) listing of dabrafenib (in combination with trametinib). MSAC noted that Stage III resected melanoma patients are at high risk of relapse and standard of care is routine follow-up. At present, no effective adjuvant therapies are available on the PBS.

MSAC noted that, at its April 2018 meeting, PASC supported expanding the current population within existing MBS item 73336, as opposed to creating a new MBS item. PASC also recommended that the application be considered by the MSAC Executive for a streamlined process pathway.

MSAC noted that, at the July 2019 PBAC meeting, the PBAC made a positive recommendation to amend the PBS listing for dabrafenib and trametinib to include the adjuvant treatment of patients who have had complete surgically resected *BRAF* V600 mutation positive Stage IIIB, IIIC or IIID malignant melanoma. MSAC advised that the removal of the word "unresectable" from the descriptor for MBS item 73336 would be sufficient to extend MBS item 73336 to complement this PBAC recommendation by including patients with completely resected Stage III metastatic cutaneous melanoma.

The PBAC recommendation was for stage IIIB, IIIC or IIID tumour with the exclusion of micrometastatic disease IIIA It is proposed that the Department consider the inclusion of a clarifying practice note with the proposed descriptor.

MSAC noted that the MSAC Executive had recently opposed the option of replacing dabrafenib, vemurafenib and encorafenib with a generic descriptor (for example, "*BRAF* inhibitor therapies listed on the PBS"), because "the nomenclature and interpretation for the drug class is not precise or agreed on by all stakeholders".

MSAC recalled that it had previously advised that the *BRAF* V600 mutation test listed in MBS item 73336 is safe, clinically effective and cost-effective in later stage melanoma.

MSAC noted that the submission suggested that around **redacted** "additional" patients with resected Stage III melanoma would be eligible for *BRAF* testing per year ($230.95 per patient; $**redacted** in total) with around **redacted** found positive and eligible for treatment. The figure of **redacted** was obtained via a survey of 31 oncologists who estimated that **redacted**% of patients with Stage III disease would undergo nodal resection. However, MSAC considered that these calculations do not take into account the change in timing of the test; a subset of these patients would no longer require testing in the "unresectable" or metastatic setting down the track, so the requested testing would not be all additive to the status quo (that is, the increase in testing would be somewhat smaller than estimated).

MSAC considered whether *BRAF* testing should be pathologist-determinable, if required, in the adjuvant setting. Currently, it is an add-on request required from a clinician (creating additional delay), whereas *BRAF* testing could be expedited following diagnosis of a nodal or

distant metastasis if it were pathologist-determinable. However, MSAC noted that this could be too complicated in practice, and so did not support this testing becoming pathologist-determinable.

MSAC noted that this is the first adjuvant application for this type of combination therapy and that other currently listed or future *BRAF* inhibitor combinations would require additional successful PBAC application to extend coverage to adjuvant therapy in resected Stage III melanoma.

4. Background

The other part of the streamlined codependent submission was lodged in November 2018 to extend the listing of dabrafenib in combination with trametinib (dabrafenib+trametinib) on the Pharmaceutical Benefits Scheme (PBS), to be used as an adjuvant therapy for patients with *BRAF* V600 mutation positive, completely resected Stage III melanoma. This submission was deferred at the March 2019 PBAC meeting. Novartis subsequently lodged a minor resubmission which was considered at the July 2019 PBAC meeting.

5. Prerequisites to implementation of any funding advice

Confirmation of *BRAF* V600 mutation using an approved/validated test is required for selection of patients appropriate for dabrafenib+trametinib, as per the approved TGA indications:

- the treatment of patients with *BRAF* V600 mutation positive unresectable Stage III or metastatic (Stage IV) melanoma; and
- adjuvant treatment of patients with a *BRAF* mutation and involvement of the lymph node(s), following complete resection.

6. Proposal for public funding

The application proposed that the term 'unresectable' be removed from the current item descriptor, to expand access to include patients with Stage III resected melanoma:

Table 1 Proposed amendment to MBS item 73336

Category 6 – PATHOLOGY SERVICES
Proposed item descriptor: A test of tumour tissue from a patient with ~~unresectable~~ Stage III or Stage IV metastatic cutaneous melanoma, requested by, or on behalf of, a specialist or consultant physician, to determine if the requirements relating to BRAF V600 mutation status for access to dabrafenib or vemurafenib under the Pharmaceutical Benefits Scheme are fulfilled. Fee: $230.95

7. Proposed intervention's place in clinical management

Inclusion of patients with Stage III resected melanoma to the MBS item descriptor was expected to extend access to adjuvant dabrafenib+trametinib on the PBS, which the application claimed would significantly reduce the risk of disease recurrence in patients with Stage III *BRAF* positive melanoma, leading to improved overall survival and quality of life.

8. Financial/budgetary impacts

An epidemiological approach was used to estimate the number of additional patients eligible for *BRAF* mutation testing on the MBS (Table 2).

Table 2 Estimated number of additional patients eligible for BRAF mutation testing

		2019	2020	2021	2022	2023	2024
A	Total stage III	redacted	redacted	redacted	redacted	redacted	redacted
B = A* redacted %[1]	Stage III resected	redacted	redacted	redacted	redacted	redacted	redacted
C = B*44.5%[2]	Stage III resected *BRAF*+	redacted	redacted	redacted	redacted	redacted	redacted

Source: Table 1, p2 of Minor Submission
[1]Market research survey of 31 medical oncologists
[2]Menzies et al 2012

The application's estimated additional costs to the MBS for *BRAF* mutation testing are summarised in Table 3.

Table 3 Estimated additional costs to the MBS for BRAF mutation testing

	2019	2020	2021	2022	2023	2024
Total MBS cost, 100% scheduled fee	$ redacted	$ redacted	$ redacted	$ redacted	$ redacted	$ redacted
Total MBS cost, 85% scheduled fee	$ redacted	$ redacted	$ redacted	$ redacted	$ redacted	$ redacted

Source: Table 2, p2 of Minor Submission

9. Applicant's comments on MSAC's Public Summary Document

Novartis welcomes MSAC's decision to broaden the existing MBS item for *BRAF* V600 testing to include Stage III resected melanoma patients for access to dabrafenib and trametinib on the PBS.

10. Further information on MSAC

MSAC Terms of Reference and other information are available on the MSAC Website: visit the MSAC website